Bladder Cancer in Nonsmokers

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Potential risk factors for bladder cancer were studied in a series of 76 male and 76 female bladder cancer cases and 238 male and 254 female controls who reported never having smoked. Risk factors included usual occupation, smoking by the spouse, sidestream smoke exposure at home and at work and in transportation, coffee drinking (caffeinated and decaffeinated), artificial sweetener use, body mass index, and a history of diabetes and high blood pressure. No association was found with spouse's smoking or reported sidestream smoke exposure, coffee drinking, artificial sweetener use, or a number of other variables; however, there was some indication that several occupations were overrepresented in the cases. A positive association was found with snuff use in women, but the numbers were small (three cases and one control). Restriction of the study to lifetime nonsmokers permitted the assessment of potential risk factors in the absence of potential confounding and interactive effects of smoking. The study had adequate statistical power to detect moderately small elevated risks due to the main factors examined.

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CIGARETTE SMOKING is a well-established risk factor for bladder cancer, as is occupational exposure to specific carcinogens[1-3]; however, it is generally agreed that a substantial proportion of bladder cancer incidence remains unexplained.[4-6]

In the current study, a number of potential risk factors for bladder cancer are examined in a group of bladder cancer cases and controls who reported never having smoked on a regular basis (*e.g.*, as much as one cigarette, cigar, or pipe per day for 1 year). The restriction of the study to lifetime nonsmokers permits the assessment of potential risk factors in the absence of smoking, which could act as a confounding variable.

Methods

The data used in this analysis derive from a large, ongoing case-control study of smoking and cancer that has been in progress since 1969, as previously described.[7] In this large study, cases consisted of patients with tobacco-related cancers who were interviewed in 18 hospitals in six U. S. cities. Controls were hospitalized patients with current diagnoses of non-tobacco-related diseases and were interviewed in the same hospitals during the same time period, thus providing a pool of controls.

In the current study, all bladder cancer cases interviewed between 1976 and 1983 were selected from the large data base. There was a total of 751 male and 197 female bladder cancer cases during this period. Seventy-six male and 76 female bladder cancer cases reported never having smoked regularly. For each of these never-smoking cases, three controls were sought in the large pool of hospitalized controls. The controls were matched on age (within 5 years), sex, race, hospital, year of interview, and lifetime nonsmoking status. In all, 238 male and 254 female controls were selected (3 controls were not obtained for all cases).

The distribution of diagnoses among the controls was as follows: men, 67.1% non-tobacco-related cancers, 32.9% noncancer diagnoses; women, 59.3% non-tobacco-related cancers, 40.7% noncancer.

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TABLE 1. Distribution of Nonsmoking Bladder Cancer Cases and Controls by Selected Demographic Variables

	M				F			
	Cases		Controls		Cases		Controls	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Age								
≤49	15	(19.7)	50	(21.0)	5	(6.6)	20	(7.9)
50–59	20	(26.3)	55	(23.1)	9	(11.8)	30	(11.8)
60–69	30	(39.5)	104	(43.7)	32	(42.1)	116	(45.7)
70+	11	(14.5)	29	(12.2)	30	(39.5)	88	(34.6)
Total	76		238		76		254	
Religion								
Protestant	20	(26.3)	63	(26.5)	29	(38.2)	70	(27.6)
Catholic	29	(38.2)	94	(39.5)	34	(44.7)	125	(49.2)
Jewish	21	(27.6)	60	(25.2)	7	(9.2)	40	(15.7)
Other	6	(7.9)	21	(8.8)	6	(7.9)	19	(7.5)
Total	76		238		76		254	
Years of education*								
1–11	14	(18.7)	47	(20.0)	40	(54.1)	104	(41.4)
12	16	(21.3)	54	(23.0)	16	(21.6)	87	(34.7)
13–15	11	(14.7)	41	(17.4)	8	(10.8)	29	(11.6)
16+	34	(45.3)	93	(39.6)	10	(13.5)	31	(12.3)
Total	75		235		74		251	
Occupational status								
Professional	39	(51.3)	117	(49.2)	11	(14.5)	37	(14.5)
Skilled	22	(29.0)	82	(34.4)	17	(22.4)	86	(33.9)
Semiskilled	9	(11.8)	23	(9.7)	5	(6.6)	16	(6.3)
Unskilled	6	(7.9)	16	(6.7)	8	(10.5)	26	(10.2)
Housewife	—	—	—	—	35	(46.0)	89	(35.0)
Total	76		238		76		254	

* Years of education unknown for one male case, two female cases, three male controls, and three female controls.

All subjects were interviewed in the hospital with a structured questionnaire, which contained questions on demographic factors, residence, usual occupation, self-reported occupational exposures, tobacco smoking, spouse's smoking, exposure to sidestream tobacco smoke, alcohol use, coffee drinking, saccharin use, height, current weight, weight 5 years before current hospitalization, and history of previous diseases.

Usual occupation was assessed by asking each subject what job he had held for the longest period of time. Self-reported occupation was coded according to an abbreviated list of the U. S. Bureau of Census codes.[8] Information on exposure at work or at home to a variety of occupational and environmental substances was elicited from each subject. An individual was classified as exposed to a specific substance if that exposure occurred for at least 8 hours/week for at least 1 year. The number of years of each self-reported exposure was also obtained. Residence at three periods (childhood, adolescence, adulthood) was categorized as urban, rural, or mixed urban and rural. The county and state of longest residence in adulthood was also obtained from those interviewed from 1979 onward.

Information on spouse's smoking status was asked of those individuals who had ever been married. Because questions on passive smoking were added to the questionnaire in 1979, spouse's smoking status was available for only 58% of the nonsmoking bladder cancer cases and controls. Information on exposure to sidestream smoke at home and at work was available for only 21% of the cases and controls.

Usual intake of regular and decaffeinated coffee was determined by asking for the number of cups of each kind drunk per day.

Artificial sweetener use was elicited in terms of whether the subject had ever used either saccharin or cyclamate, as well as number of packets, tablets, or drops consumed per day of saccharin food additives; number of cans consumed per day of artificially sweetened beverages; and years of artificial sweetener use.

Body mass index (BMI) (weight/height^2 × 10,000) was calculated for each subject with the reported weight of 5 years before diagnosis.

History of diabetes mellitus and of high blood pressure was also obtained from each subject.

The measure of association used to examine the rela-

TABLE 2. Selected Occupations of Male Nonsmoking Bladder Cancer Cases and Controls

Usual occupation	Cases No.	Cases (%)*	Controls No.	Controls (%)†	Odds ratio
Auto mechanics	0	(0.0)	5	(2.1)	0.3
Chemical workers	4	(5.3)	2	(0.8)	6.6‡
Construction workers	0	(0.0)	7	(2.9)	0.2
Electrical workers	2	(2.6)	6	(2.5)	1.1
Farmers	3	(3.9)	1	(0.4)	9.7‡
Firemen	3	(3.9)	0	(0.0)	22.7‡
Machinists	4	(5.3)	3	(1.3)	4.4‡
Physicians	6	(7.9)	2	(0.8)	10.1‡
Policemen	0	(0.0)	5	(2.1)	0.3
Printers	2	(2.6)	6	(2.5)	1.1
Textile workers	0	(0.0)	3	(1.3)	0.4
Truck, bus, taxi drivers	3	(3.9)	8	(3.4)	1.2
Woodworkers	2	(2.6)	1	(0.4)	6.4

* Based on 76 cases.
† Based on 238 controls.
‡ Statistically significant at $P = 0.05$ level.

tionship between variables of interest and bladder cancer is the odds ratio.[9] Corresponding test-based 95% confidence intervals were calculated according to Miettinen.[10]

Results

Information on cell type was available for all nonsmoking bladder cancer cases. The distribution of cell types among the cancer cases was as follows: men, 93.4% transitional cell carcinoma, 3.9% adenocarcinoma, 2.6% squamous cell carcinoma; women, 82.7% transitional cell carcinoma, 6.7% adenocarcinoma, 6.7% squamous cell carcinoma, 2.6% anaplastic, 1.3% papillary and mucinous adenocarcinoma.

The age distributions of the bladder cancer cases and controls are presented in Table 1. Few differences were found between cases and controls with respect to age, because the controls were roughly matched to cases on this variable. Female cases and controls were older, in general, than male cases and controls; mean age of female cases was 66.4 years, compared with 58.9 years for male cases.

Cases and controls differed little by religious affiliation, years of education, or occupational status as derived from self-reported occupational title (Table 1). The large number of subjects classified as professional or managerial reflects the relatively high socioeconomic level of male patients from Memorial Sloan-Kettering, the hospital contributing the most patients to the study population (61% of the men and 45% of the women were from Memorial).

Table 2 presents the frequency distributions of male cases and controls by selected occupations. Although the numbers are extremely small, significantly increased odds ratios for bladder cancer were found among those classified as chemical workers (primarily chemists and chemical engineers), firemen, machinists, and physicians. The increased risk found in physicians is most likely due to selective referral of physicians with bladder cancer seeking treatment at Memorial Sloan-Kettering (only one of the six physician cases was not treated at Memorial).

Among those individuals who had ever been married, bladder cancer cases and controls differed little with respect to whether or not their spouse smoked. Fifteen of the 49 male cases (30.6%) had a wife who had smoked, compared to 50 of the 137 male controls (36.5%). Among women, 24 of the 35 cases (68.6%) had a husband who had smoked compared with 83 of the 129 controls (64.8%). Male cases were somewhat more likely than controls to report exposure to sidestream smoke at home, whereas female cases were less likely to report home exposure (Table 3). These differences were small and did not reach statistical significance. When exposure to sidestream smoke at work or in transportation was examined (Table 4), male cases reported less exposure, whereas female cases reported more exposure than their corre-

TABLE 3. Number of Hours Per Week of Exposure to Sidestream Tobacco Smoke at Home* in Nonsmoking Bladder Cancer Cases and Controls

Hours/week	M Cases No.	M Cases (%)	M Controls No.	M Controls (%)	F Cases No.	F Cases (%)	F Controls No.	F Controls (%)
None	16	(69.6)	34	(77.3)	11	(64.7)	15	(53.6)
<1	1	(4.4)	0	(0)	1	(5.9)	0	(0)
1–2	0	(0)	1	(2.3)	0	(0)	0	(0)
3–4	2	(8.7)	0	(0)	0	(0)	0	(0)
5–9	4	(17.4)	8	(18.2)	1	(5.9)	1	(3.6)
10+	0	(0)	1	(2.3)	4	(23.5)	12	(42.9)
	23		44		17		28	

* This information is available only for those subjects interviewed from 1979 to 1981. The ratio of cases to controls in this table is closer to 1:2 (rather than the 1:3 ratio in other tables) due to the fact that the questionnaire containing this item was given only to a limited number of controls, whereas the remaining items were asked of the entire pool of controls.

TABLE 4. Number of Hours Per Week of Exposure to Sidestream Tobacco Smoke at Work and in Transportation* in Nonsmoking Bladder Cancer Cases and Controls

	M				F			
	Cases		Controls		Cases		Controls	
Hours/week	No.	(%)	No.	(%)	No.	(%)	No.	(%)
None	12	(52.2)	18	(40.9)	11	(64.7)	23	(82.1)
<1	0	(0)	1	(2.3)	0	(0)	0	(0)
1–2	0	(0)	1	(2.3)	0	(0)	0	(0)
3–4	1	(4.4)	3	(6.8)	0	(0)	1	(3.6)
5–9	4	(17.4)	4	(9.1)	1	(5.9)	0	(0)
10+	6	(26.1)	16	(36.4)	5	(29.4)	4	(14.3)
Don't know	0	(0)	1	(2.3)	0	(0)	0	(0)
	23		44		17		28	

* This information is available only for those subjects interviewed from 1979 to 1981. The ratio of cases to controls in this table is closer to 1:2 (rather than the 1:3 ratio in other tables) due to the fact that the questionnaire containing this item was given only to a limited number of controls, whereas the remaining items were asked of the entire pool of controls.

sponding controls. Again, these differences were not statistically significant.

The distribution of cases and controls by the number of cups of brewed coffee consumed per day are presented in Table 5. None of the odds ratios for drinkers of varying numbers of cups per day was significantly elevated, and there was no suggestion of a trend in either sex. Daily consumption of decaffeinated coffee also showed no association with bladder cancer (Table 6). Cases and controls were similar with respect to daily intake of tea and instant coffee (data not shown).

Among the men, 77.6% of the cases and 80.2% of the controls never used artificial sweeteners, whereas 76.3% of the cases and 79.4% of the controls never drank diet soda. Among the women, the cases were slightly less likely than the controls to use artificial sweeteners or diet drinks (79.0% of the cases, *versus* 76.0% of the controls never used artificial sweeteners, and 84.2% of the cases, compared with 77.2% of the controls, never drank diet soda).

No association with bladder cancer risk was found for BMI, or a history of diabetes or of high blood pressure.

Only one female case and one male case chewed tobacco, and no male cases reported ever having used snuff. Snuff use among women, however, was positively associated with bladder cancer; three cases, compared with one control, had ever used snuff (Fisher's Exact Test, $P = 0.04$). Of the four female snuff users, one case was a current user, and the remaining two cases and one control were exusers. Two cases use or had used snuff constantly; the remaining case used snuff more than 10 times/week, whereas the one control used snuff less than once a week. The three cases used snuff for 1, 31, and 48 years, respectively, whereas the control used snuff for 3 years.

Other variables examined and found not to be associated with bladder cancer included: marital status; place of birth (foreign- or U. S.-born); residence in childhood, adolescence, or adulthood with respect to urban or rural environment; county of longest residence in adulthood; self-reported exposure to a variety of substances; and consumption of wine, beer, and hard liquor.

Discussion

The examination of a variety of possible risk factors for bladder cancer in a homogeneous group of lifetime nonsmokers provided a means of eliminating the potential confounding and interactive effects of smoking, already

TABLE 5. Usual Intake of Brewed Coffee Among Nonsmoking Bladder Cancer Cases and Controls

	M				F			
No. of cups/day	Cases	Controls	OR	95% CI	Cases	Controls	OR	95% CI
None/occasional	40	129	1.00*	—	40	146	1.00*	—
1–2	18	64	0.91	0.48–1.71	24	58	1.51	0.84–2.72
3–4	15	35	1.38	0.69–2.79	8	36	0.81	0.35–1.88
5–6	3	7	1.38	0.34–5.59	2	11	0.66	0.14–3.10
7+	0	3	0.46	0.03–8.47	2	3	2.43	0.41–14.34
	76	238			76	254		

* Referent group.

OR: odds ratio; CI: confidence interval.

TABLE 6. Current Usual Intake of Decaffeinated Coffee Among Nonsmoking Bladder Cancer Cases and Controls

	M				F			
No. of cups/day	Cases	Controls	OR	95% CI	Cases	Controls	OR	95% CI
None/occasional	60	179	1.00*	—	62	180	1.00*	—
1–2	14	39	1.07	0.54–2.11	9	52	0.50	0.24–1.07
3–4	2	15	0.40	0.09–1.71	5	20	0.73	0.26–2.01
5+	0	5	0.27	0.02–4.10	0	2	0.58	0.03–11.82
	76	238			76	254		

* Referent group.

OR: odds ratio; CI: confidence interval.

established as a major risk factor for the disease. The relatively small number of nonsmoking male and female bladder cancer cases resulted in small numbers when studying subgroups; however, the study had sufficient power to detect moderately small associations. For a variable for which information was available on all study participants, such as decaffeinated coffee use, with an exposure rate in the controls of 30% and an alpha value of 0.05, the power to detect an odds ratio of 1.67 was 90%. For a variable with information missing for some study subjects, such as spouse's smoking in men, the power to detect an odds ratio of 1.5, given an exposure rate in the controls of 36.5% and an alpha of 0.05, was 58%. For spouse's smoking in women with an exposure rate of 65% in the controls, the power to detect an odds ratio of 1.3 was 67%.

The role of occupation in the etiology of bladder cancer has been extensively studied,[11–16] and it has been estimated that as much as 30% of bladder cancer cases may have an occupationally related cause.[17] Elevated risks among chemical workers, machinists, and farmers have been found in some previous studies,[6,12,14,15,18–20] whereas others have not confirmed these findings.[12,13,15,16] Whether the observed elevated risk of bladder cancer in firefighters is due to a common exposure such as smoke inhalation requires further study. There was some suggestion of an increased risk in firemen in a mortality study in Washington State,[16] although the numbers were small. By considering only nonsmokers, the current analysis precludes the chance of showing an interaction between smoking, occupation, and bladder cancer, a possibility suggested by Vineis and colleagues.[21]

The findings of the current study with respect to occupation are limited for several reasons. First, because of the composition of our hospital population (largely middle-class and professional), blue collar industrial occupations are underrepresented. Furthermore, the number of subjects in any one occupational group was small. An additional consideration is that because of the many comparisons made, some may be due to chance alone; however, it is unlikely that all of these findings resulted from chance. As mentioned previously, the association found with physicians is most likely due to referral bias. The physicians did not share a common specialty and have been examined previously and not shown to have an excess risk of bladder cancer.[16] No associations were found between occupation and bladder cancer among the women.

Passive inhalation has recently become a subject of considerable interest, particularly as it relates to lung cancer risk.[22] Because active smoking is a risk factor for bladder cancer, it may be possible that heavy exposure to sidestream smoke increases the risk of bladder cancer in nonsmokers. The possibility of a relationship between passive inhalation and bladder cancer receives some support from studies in which elevated levels of nicotine or cotinine (a metabolite of nicotine)[23–26] or mutagens[27] have been measured in the urine of nonsmokers passively exposed to smoke. The results of the current study did not suggest greater exposure to sidestream smoke among those with bladder cancer; however, information on passive inhalation was not available for all study subjects because of the use of a different questionnaire version early in the study. Furthermore, these questions provide only a rough estimate of current sidestream smoke exposure rather than of lifetime exposure. Future studies designed to obtain a more precise estimate of sidestream smoke exposure will be able to more clearly assess the relationship between exposure to others' smoke and the occurrence of bladder cancer.

Case-control studies that have examined the relationship of coffee consumption with bladder cancer have yielded inconsistent results. Morrison has recently reviewed these studies and concluded that the major problem in assessing the coffee–bladder cancer relationship is the difficulty of adequately controlling for confounding by cigarette smoking.[28] Of the three studies that present data on coffee consumption of nonsmokers separately, one showed little increased risk among nonsmokers,[29] one yielded an odds ratio of 1.9 for both men and women who drank 8 or more cups/week compared with drinkers of 7 or fewer cups/week,[30] and one showed an increased

risk in men but not in women.[31] Although the current study found no association between coffee drinking and bladder cancer in nonsmokers of either sex, the disparate results in these studies leave the issue unresolved.

The finding in the current study of no apparent association between either diet beverage consumption or artificial sweetener use and bladder cancer in either sex is in agreement with the results of several other case-control studies.[13,32-36] Although a slight elevation in risk among women has been shown in subgroups of nonsmokers,[32,34,37] the results among men have been inconsistent.[34,37,38]

Snuff use has not been widely examined as a risk factor for bladder cancer. Dunham and colleagues[39] reported more snuff use among their white female controls (2.5%) than among cases (0.9%). The finding of the current study that cases were more likely to use snuff than controls must be interpreted with caution in view of the extremely small number of snuff users. The relationship between snuff use and bladder cancer should be examined further with more subjects.

The etiology of bladder cancer is still largely unknown. The current study, which has examined a number of potential risk factors in the absence of the confounding and interactive effects of the major risk factor (smoking), suggests that coffee drinking, artificial sweetener use, and exposure to sidestream smoke are not important factors in bladder cancer in nonsmokers.

REFERENCES

1. U. S. Department of Health and Human Services. The Health Consequences of Smoking: Cancer. A Report of the Surgeon General. DHHS Publication No. (PHS) 82-50179. Washington, DC: Public Health Service, Office on Smoking and Health, 1982: 101–113.
2. Matanowski GM, Elliot EA. Bladder cancer epidemiology. *Epidemiol Rev* 1981; 3:203–229.
3. Morrison AS, Cole P. Urinary tract. In: Schottenfeld D, Fraumeni T, eds. Cancer Epidemiology and Prevention. Philadelphia: W. B. Saunders, 1982: 925–937.
4. Doll R, Peto R. The Causes of Cancer. New York: Oxford University Press, 1981: 1221.
5. Cole P, Monson RR, Haning H, Friedell GH. Smoking and cancer of the lower urinary tract. *N Engl J Med* 1971; 284:129–134.
6. Wynder EL, Goldsmith R. The epidemiology of bladder cancer: A second look. *Cancer* 1977; 40:1246–1268.
7. Wynder EL, Stellman SD. Comparative epidemiology of tobacco-related cancers. *Cancer Res* 1977; 37:4608–4622.
8. U. S. Department of Commerce. U. S. Bureau of Census: Detailed Characteristics. Final Report, U. S. Summary. Publication No. PC(1)-D1. Washington, DC: U. S. Government Printing Office, 1973; Table 226.
9. Fleiss JL. Statistical Methods for Rates and Proportions, ed. 2. New York: John Wiley and Sons, 1981; 181–193.
10. Rothman KJ, Boice JD. Epidemiologic Analysis with a Programmable Calculator. Washington, DC: U. S. DHEW, Public Health Service Publication No. (NIH) 79-1649, 1979.
11. Wynder EL, Onderdonk S, Mantel N. An epidemiological investigation of cancer of the bladder. *Cancer* 1963; 16:1388–1407.
12. Cole P, Hoover R, Friedell GH. Occupation and cancer of the lower urinary tract. *Cancer* 1972; 29:1250–1260.
13. Najem GR, Louria DB, Seebode JJ *et al.* Lifetime occupation, smoking, caffeine, saccharine, hair dyes, and bladder carcinogenesis. *Int J Epidemiol* 1982; 11:212–217.
14. Howe GR, Burch JD, Miller AB *et al.* Tobacco use, occupation, coffee, various nutrients, and bladder cancer. *J Natl Cancer Inst* 1980; 64:701–713.
15. Decoufle P, Stanislawczyk K, Houten L, Bross ID, Viadana E. A retrospective survey of cancer in relation to occupation. Washington, DC: U. S. Government Printing Office, DHEW Publication No. (NIOSH) 77-178, 1977.
16. Milham S. Occupational mortality in Washington State 1950–1970, vol. 1. Washington, DC: U. S. Government Printing Office, DHEW Publication No. (NIOSH) 76:175–176, 1976.
17. Higginson J. Proportion of cancers due to occupation. *Prev Med* 1980; 9:180–188.
18. Gottlieb MS, Pickle LW. Bladder cancer mortality in Louisiana. *J La State Med Soc* 1981; 133:6–9.
19. Miller CT, Neutel CI, Nair RC, Marrett LD, Last JM, Collins WE. Relative importance of risk factors in bladder carcinogenesis. *J Chronic Dis* 1978; 31:51–56.
20. Glashan RW, Cartwright RA. Occupational bladder cancer and cigarette smoking in West Yorkshire. *Br J Urol* 1981; 53:602–604.
21. Vineis P, Segnan N, Costa G, Terracini B. Evidence of a multiplicative effect between cigarette smoking and occupational exposures in the aetiology of bladder cancer. *Cancer Lett* 1981; 14:285–290.
22. Kabat GK, Wynder EL. Lung cancer in nonsmokers. *Cancer* 1984; 53:1214–1221.
23. Matsukura S, Taminato T, Kitano N *et al.* Effects of environmental tobacco smoke on urinary cotinine excretion in nonsmokers: Evidence for passive smoking. *N Engl J Med* 1984; 311:828–832.
24. Greenberg RA, Haley NJ, Etzel RA, Loda FA. Measuring the exposure of infants to tobacco smoke: Nicotine and cotinine in urine and saliva. *N Engl J Med* 1984; 310:1075–1078.
25. Feyerabend C, Higenbottam T, Russell MAH. Nicotine concentrations in urine and saliva of smokers and non-smokers. *Br Med J* 1982; 284:1002–1004.
26. Russell MAH, Feyerabend C. Blood and urinary nicotine in non-smokers. *Lancet* 1975; 1:179–181.
27. Bos RP, Theuws JLG, Henderson PTH. Excretion of mutagens in human urine after passive smoking. *Cancer Lett* 1983; 19:85–90.
28. Morrison AS. Control of cigarette smoking in evaluating the association of coffee drinking and bladder cancer. In: MacMahon B, Sugimura T, eds. Coffee and Health, Banbury Report 17. Cold Spring Harbor Laboratory, 1984; 127–136.
29. Bross IDJ, Tidings J. Another look at coffee drinking and cancer of the urinary bladder. *Prev Med* 1973; 2:445–451.
30. Marrett LD, Walter SD, Meigs JW. Coffee drinking and bladder cancer in Connecticut. *Am J Epidemiol* 1983; 117:113–127.
31. Hartge P, Hoover R, West DW, Lyon JL. Coffee drinking and risk of bladder cancer. *J Natl Cancer Inst* 1983; 70:1021–1026.
32. Morrison AS, Buring JE. Artificial sweeteners and cancer of the lower urinary tract. *N Engl J Med* 1980; 302:537–541.
33. Silverman DT, Hoover RN, Swanson GM. Artificial sweeteners and lower urinary tract cancer: Hospital *vs.* population controls. *Am J Epidemiol* 1983; 117:326–334.
34. Hoover RN, Strasser PH. Artificial sweeteners and human bladder cancer: Preliminary results. *Lancet* 1980; 1:837–840.
35. Wynder EL, Stellman SD. Artificial sweetener use and bladder cancer: A case–control study. *Science* 1980; 207:1214–1216.
36. Kessler I. Non-nutritive sweeteners and human bladder cancer: Preliminary findings. *J Urol* 1976; 115:143–146.
37. Cartwright RA, Adib R, Glashan R, Gray BK. The epidemiology of bladder cancer in West Yorkshire: A preliminary report on non-occupational aetiologies. *Carcinogenesis* 1981; 2:343–347.
38. Miller AB, Howe GR. Artificial sweeteners and bladder cancer (letter). *Lancet* 1977; 2:1221–1222.
39. Dunham LJ, Rabson AS, Stewart HL, Frank AS, Young JL. Rates, interview, and pathology study of cancer of the urinary bladder in New Orleans. *J Natl Cancer Inst* 1968; 41:683–709.